Remarks

Claims 1 to 10 are pending in the instant application. Claims 6 and 7 have been amended. The Applicants amended the title of the invention to clearly indicate the invention to which the claims are directed. Applicants respectfully request reconsideration and withdrawal of the rejections for the reasons set forth herein. There is no issue of new matter.

Claim Rejections Under 35 USC §112

Claims 2 and 6 to 10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Without conceding the validity of this rejection, Applicants have elected to present the invention in different terms, which terms obviate the asserted basis for this rejection. Applicants respectfully assert that due to the discussion and amendments made to the existing claims, this rejection is now traversed. Specifically, Applicants have amended claims 6 and 7, to more particularly point out and distinctly claim that which Applicants regard as the subject matter of their invention. The amendments are fully supported by the specification.

Regarding Claim 2, the Examiner asserts that "the term 'prevalent' is a relative term which renders the claim indefinite." Furthermore, the Examiner states that "prevalent" is "not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention." The Applicants respectfully disagree.

In Claim 2, the phrase "meningococcal strain with a serosubtype that is prevalent in a country of use" is defined in the present specification, for example, on page 4, line 10-24. The text states:

> By a "meningococcus strain with a serosubtype that is prevalent in a country of use" it is meant the bleb is derived from a meningococcal strain with a serosubtype which is most prevalent (or possibly second or third or fourth prevalent – particularly if 2 or 3 or 4 bleb preparations with homologous bactericidal activity are incorporated in the vaccine) in percentage terms amongst strains of all serosubtypes which cause meningococcal disease in the country (or region or continent) – i.e. strains isolated during laboratory-based active surveillance of meningococcal disease in a country,

> region or continent. Preferably the serosubtype of such a bleb constitutes more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 30, 40, 50 or 60 % of all serosubtypes which cause meningococcal disease in the country (or region or continent).
>
> If one bleb preparation with homologous bactericidal activity is included in the composition it is preferred that it is derived from a strain with a subserotype which is most prevalent in the country (or region or continent), if two or three or four are included then it is preferred that the strains used cover the two or three or four (respectively) most prevalent subserotypes.

Therefore, the specification does provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would be reasonably apprised of the scope of the invention.

The Examiner rejected Claim 6, for reciting the broad range neisserial together with the narrow range of meningococcal. Applicants amended the preamble of Claim 6 to neisserial diseases which includes the narrower scope of meningococcal disease.

In addition, the Examiner rejected Claim 7, for being vague and indefinite by the phrase "capsular polysaccharides selected from the following serotypes: A, C, Y and W" because the art and present specification exemplify "serogroups" A, C, Y, and W. The Applicants amended Claim 7 to replace serotypes with serogroups to clarify the variations in the meningococcal capsular polysaccharide.

In view of the forgoing remarks, the Applicants respectfully submit that they have overcome all grounds of the Examiner's rejection under 35 U.S.C. §112, second paragraph, and that rejections should be withdrawn.

Claim Rejections Under 35 USC §102

Claims 1 to 9 are rejected under 35 USC 102 (b) as being anticipated by Berthet, *et al.* (WO 01/09350). The Applicants respectfully traverse this rejection to the extent that it applies to the present claims and assert that this rejection is an improper 35 USC § 102 rejection. Section 102(b) requires that "each and every element as set forth in the claim be found, either expressly or inherently described, in a single prior art reference." *Constant v. Advanced Micro-Devices, Inc.*, 848 F.2d 1560, 1570, 7 U.S.P.Q.2d 1057 (Fed. Cir.), *cert. denied*, 488 U.S. 892 (1988).

Berthet, *et al.* does not teach or even suggest a multivalent meningococcal bleb composition comprising a bleb preparation deficient in PorA in that it has less than 80% of the amount of PorA as compared to the same quantity of blebs made from strain H44/76 and a bleb preparation that is not deficient in PorA compared to blebs made from strain H44/76.

The Examiner suggests that Berthet, *et al.* teach vaccines comprising mixtures of bleb preparations from 2 or more strains, including serotypes P1.15, P1.7,16, and P1.4. The Examiner further notes that Berthet, *et al.* anticipates the instantly claimed invention because the instant invention discloses that P1.15 is the serosubtype of strain CU-385, which has 20% PorA and that P1.7,16 is the serosubtype of strain H44/76, which has 30% PorA. The Applicants disagree and assert that Berthet, *et al.* discloses the combination of 2 or more blebs isolated from meningococcal strains selected from serosubtypes P1.15, P1.7,16, P1.4 and P1.2. The Applicants emphasize that CU-385 is a species of all meningococcal strains of the serosubtype genus P1.15. CU-385 happens to be deficient in PorA. This is not to say the whole genus of strains of serosubtype P1.15 consists of strains that are similarly deficient. Berthet, *et al.* merely discloses the fact that any member of the P1.15 genus can be mixed with other blebs. In Berthet, *et al.,* there is no disclosure nor motivation for a skilled person to select a member of the genus which is deficient in PorA in a multivalent vaccine. For that reason, the present claims must be novel over Berthet, *et al.*

In view of the forgoing remarks, the Applicants respectfully submit that they have overcome all grounds of the Examiner's rejection under 35 U.S.C. §102(b) relating to Berthet *et al.* and that the rejection is improper and should be withdrawn.

Claims 1 to 9 are rejected under 35 USC §102(b) as anticipated by or, in the alternative, under U.S.C. §103(a) as obvious over Granoff, *et al.* (WO 02/09643). The Applicants respectfully traverse this rejection to the extent that it applies to the present claims and assert that this rejection is an improper 35 USC §102 and 35 USC §103 rejection. Section 102(b) requires that "each and every element as set forth in the claim be found, either expressly or inherently described, in a single prior art reference." *Constant v. Advanced Micro-Devices,*

Inc., 848 F.2d 1560, 1570, 7 U.S.P.Q.2d 1057 (Fed. Cir.), *cert. denied*, 488 U.S. 892 (1988).

Granoff, *et al.* does not teach or even suggest a multivalent meningococcal bleb composition comprising a bleb preparation deficient in PorA in that it has less than 80% of the amount of PorA as compared to the same quantity of blebs made from strain H44/76 and a bleb preparation that is not deficient in PorA compared to blebs made from strain H44/76.

In addition, the compositions in Granoff, *et al*. differ from the presently claimed compositions because there is no disclosure of a composition comprising blebs deficient in PorA with blebs which are not. Instead, the Granoff, *et al*. disclosure shows no concern for the level of PorA in his bleb compositions. The importance is not taught or even recognized.

Furthermore, Granoff, *et al*. concentrates on describing how the serial (or sequential) administration of different blebs gives a better immune response than when blebs are mixed in a single composition. See, for example, page 48, beginning at line 20 and Figure 8 where three different meningococcal blebs are administered serially (Chori) or at the same time (Chori Mix). In terms of killing strain CU-385, antibodies after Chori induce high levels of bactericidal antibodies, but after Chori Mix no bactericidal antibodies are induced (the same as the negative control).

With regard to the obviousness rejection, not only does Granoff, *et al*. not motivate the skilled person to use blebs deficient in PorA in compositions comprising two or more blebs, Granoff, *et al*. teaches away from the presently claimed invention. Granoff, *et al*. teaches one skilled in the art that the use of sequential administration of blebs (rather than mixtures) is the preferred embodiment. For example, at the bottom of page 48 and Figure 8 it is show that sequential administration was better than mixing different blebs in terms of bactericidal activity against strains CU-385 and 1000.

Therefore, it would not have been *prima facie* obvious to a person skilled in the art at the time of the invention to use any strain with serosubtypes P1.15 (and particularly not one P1.15 strain deficient in PorA) and P1.7,16 in the manufacture of a vaccine comprising a mixture blebs in order to obtain the advantage of broad spectrum protective immunity, as suggested by the Examiner.

In view of the forgoing remarks, the Applicants respectfully submit that they have overcome all grounds of the Examiner's rejection under 35 U.S.C. §102(b) and 35 U.S.C. §103(a) relating to Granoff, *et al.* and that the rejections are improper and should be withdrawn.

Claim Rejections Under 35 USC §103

Claims 1 to 10 are rejected under 35 USC 103 (a) as being unpatentable over Berthet *et al.* (WO 01/09350) in view of Lehmann *et al.* (APMIS 99:769-772 1999).

Applicants respectfully traverse. As will be recognized, claims cannot be found obvious in view of a combination of references unless the prior art itself suggests the desirability of the combination. *Berghauser v. Dann*, 204 U.S.P.Q. 393 (D.D.C. 1979); *ACS Hospital Systems, Inc. v. Montefiore Hospital*, 221 U.S.P.Q. 929 (Fed. Cir. 1984). There must be something in the prior art that would have motivated persons of ordinary skill to make the combination. *In re Stencel*, 4 U.S.P.Q.2d 1071, 1073 (Fed. Cir. 1987), *accord*, *Ex parte Marinaccio*, 10 U.S.P.Q.2d 1716 (Pat. Off. Bd. App. 1989) (combining references is improper absent some teaching, suggestion, or motivation for the combination in the prior art). In this respect, the following statement by the Patent Office Board of Appeals is noteworthy:

> Our reviewing courts have often advised the Patent and Trademark Office that it can satisfy the burden of establishing a *prima facie* case of obviousness only by showing some objective teaching in either the prior art, or knowledge generally available to one of ordinary skill in the art, that "would lead" that individual "to combine the relevant teachings of the references." ... Accordingly, an examiner cannot establish obviousness by locating references which describe various aspects of a patent applicant's invention without also providing evidence of the motivating force that would ***impel*** one skilled in the art to do what the patent applicant has done.

Ex parte Levengood, 28 U.S.P.Q.2d 1300, 1302 (Pat. Off. Bd. App. 1993) (citations omitted; emphasis added).

Significantly, the Office Action identifies no "motivating force" that would "impel" persons of ordinary skill to combine the respective teachings of the cited references in a manner that would produce the claimed inventions. Without

the benefit of Applicants' disclosure, there would have been no reason to believe that the teachings in Berthet *et al.* in view of Lehmann *et al.* would produce the claimed multivalent meningococcal bleb composition comprising a bleb preparation deficient in PorA in that it has less than 80% of the amount of PorA as compared to the same quantity of blebs made from strain H44/76 and a bleb preparation that is not deficient in PorA compared to blebs made from strain H44/76.

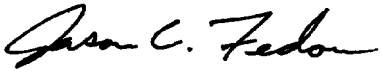
To set forth a legally sufficient *prima facie* case of obviousness, the Examiner must show that the cited references teach or suggest the claimed invention with a reasonable expectation of success. *In re Dow Chemical Co.*, 5 U.S.P.Q.2d 1529, 1531-32 (Fed. Cir. 1988). Moreover, the prior art must provide motivation to make the proposed modifications needed to arrive at the claimed invention. *In re Lalu*, 223 U.S.P.Q. 1257, 1258 (Fed. Cir. 1984). The following remarks show the nonobviousness of Applicants' claimed invention in view of the differences between the claimed invention and the cited references.

As stated above, the Applicants point out that the primary reference of Berthet *et al.* does not disclose or suggest a mixture of blebs where one is deficient in PorA. The secondary reference of Lehmann *et al.* fails to cure the deficiencies of the primary reference. As there is no discussion about the utility of PorA deficient blebs in multivalent bleb compositions in either document, there can be no motivation for a skilled person to combine these documents, and even if the documents were combined, it is submitted that a bleb composition of the instant invention would not be arrived at without hindsight.

In view of the forgoing remarks, the Applicants respectfully submit that they have overcome all grounds of the Examiner's rejections based on 35 USC §103(a) and respectfully request that this rejection be withdrawn.

The Applicants reserve the right to prosecute, in one or more patent applications, the claims to non-elected inventions, the claims as originally filed, and any other claims supported by the specification. The Applicants thank the Examiner for the Office Action and believe this response to be a full and complete response to such Office Action. Accordingly, favorable reconsideration and allowance of the pending and new claims is earnestly solicited. If it would expedite prosecution of this application, the Examiner is invited to confer with the Applicants' undersigned agent.

Respectfully submitted,



Jason C. Fedon
Agent for Applicants
Registration No. 48,138

GLAXOSMITHKLINE
Corporate Intellectual Property - UW2220
P.O. Box 1539
King of Prussia, PA 19406-0939
Phone (610) 270-6150
Facsimile (610) 270-5090